IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re application of	:	**Confirmation No. 5291**
Mie TAKAHASHI et al.	:	Attorney Docket No. 2001_1464A
Serial No.09/937,730	:	Group Art Unit 1641
Filed January 8, 2002	:	Examiner Gary W. Counts
CHROMATOGRAPHY MEDIUM AND ITS MANUFACTURING METHOD	:	**Mail Stop: Appeal Brief-Patents**

APPEAL BRIEF

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This is an appeal from the final rejection of claims 5, 12, 27, 31, 41, 45, 49, 53 and 60.

THE COMMISSIONER IS AUTHORIZED TO CHARGE ANY DEFICIENCY IN THE FEES FOR THIS PAPER TO DEPOSIT ACCOUNT NO. 23-0975

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I. REAL PARTY IN INTEREST.

The real party in interest is Matsushita Electric Industrial Co., Ltd., assignee of the entire right, title and interest to this application.

II. RELATED APPEALS AND INTERFERENCES.

There are no related prior nor pending appeals, interferences, or judicial proceedings known to Appellants, Appellants' legal representatives, or assignee which will affect or be affected by, or have a bearing on the Board's decision in the present appeal.

III. STATUS OF CLAIMS.

The status of the claims, as indicated in the Advisory Action mailed May 23, 2006, is as follows:

Claims pending: 5, 12, 27, 31, 41, 45, 49, 53 and 60

Claims rejected: 5, 12, 27, 31, 41, 45, 49, 53 and 60

Claims appealed: 5, 12, 27, 31, 41, 45, 49, 53 and 60

IV. STATUS OF AMENDMENTS.

The claims were not amended after final rejection. The last amendment to the claims was in the Amendment filed October 13, 2004.

V. SUMMARY OF THE CLAIMED SUBJECT MATTER.

The invention of claim 5 relates to a chromatography medium which comprises a reactive layer on which at least one reactive component for a chromatographic analysis is immobilized, wherein the reactive layer includes a surface active agent that is solidified when dried, and wherein the surface active agent comprises a sugar in a hydrophilic part of the surface active agent. See page 7, lines 2-8 and page 9, lines 1-4 of the disclosure.

The invention of claim 12 relates to a method for manufacturing a chromatography medium which comprises a reactive layer on which at least one reactive component for a chromatographic analysis is immobilized comprising: (a) impregnating or coating the reactive

layer of the chromatography medium with a liquid, wherein a surface active agent which is solidified when dried is dissolved in the liquid; and (b) drying the reactive layer which has been impregnated or coated with the liquid in which the surface active agent is dissolved, wherein the surface active agent comprises a sugar in a hydrophilic part of the surface active agent. See page 10, line 17 to page 11, line 2 and page 12, lines 21-25 of the disclosure.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL.

Whether claims 5, 12, 27, 31, 41, 45, 53 and 60 are unpatentable under 35 U.S.C. § 103(a) over Chu (U.S. 6,284,194) in view of Nanbu et al. (U.S. 6,130,055) or Uenoyama et al. (U.S. 5,856,117).

Whether claim 49 is unpatentable under 35 U.S.C. § 103(a) over Chu in view of Nanbu et al. or Uenoyama et al., as applied to claims 5, 12, 27, 31, 41, 45, 53 and 60, and further in view of Iwata et al. (U.S. 5,912,139).

VII. ARGUMENT.

Rejection Under 35 U.S.C. § 103(a) over Chu (U.S. 6,284,194) in view of Nanbu et al. (U.S. 6,130,055) or Uenoyama et al. (U.S. 5,856,117)

Claims 5, 12, 27, 31, 41, 45, 53 and 60 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Chu (U.S. 6,284,194) in view of Nanbu et al. (U.S. 6,130,055) or Uenoyama et al. (U.S. 5,856,117).

It is the position of the Examiner that Chu discloses an analytical device and a method of making the device, wherein the device comprises a porous reaction membrane and at least one receptor immobilized in a limited region. The Examiner states that Chu teaches applying a surfactant (surface active agent) to the reaction membrane and allowing it to dry. The Examiner further states that Chu teaches the surfactant can be polyoxyethylene (23), polyoxyethylene sorbitan monolaurate or polyoxyethylene sorbitan monooleate. The Examiner admits that Chu

fails to teach a surface active agent comprising sugar in a hydrophilic part of the surface active agent.

The Examiner asserts that Nanbu et al. and Uenoyama et al. disclose surfactants used in bioassays, and that surfactants improve assay sensitivity. The Examiner further states that Nanbu et al. and Uenoyama et al. teach the equivalence of polyoxyethylene sorbitan monolaurate and polyoxyethylene sorbitan monooleate to sucrose monolaurate surfactants (Nanbu et al.) and n-octyl-B-D-thioglucoside (Uenoyama et al.).

Therefore, the Examiner takes the position that it would have been obvious to substitute the surfactants of Nanbu et al. or Uenoyama et al. for the surfactant of Chu, because the references teach that surfactants improve assay sensitivity, and because the references show equivalence among the surfactants.

Object and Advantages of Appellants' Invention

Appellants' claim 5 recites a chromatography medium which comprises a reactive layer on which at least one reactive component for a chromatographic analysis is immobilized, wherein the reactive layer includes a surface active agent that is solidified when dried, and wherein the surface active agent comprises a sugar in a hydrophilic part of the surface active agent.

Appellants' claim 12 recites a method for manufacturing a chromatography medium which comprises a reactive layer on which at least one reactive component for a chromatographic analysis is immobilized comprising: (a) impregnating or coating the reactive layer of the chromatography medium with a liquid, wherein a surface active agent which is solidified when dried is dissolved in the liquid; and (b) drying the reactive layer which has been impregnated or coated with the liquid in which the surface active agent is dissolved, wherein the surface active agent comprises a sugar in a hydrophilic part of the surface active agent.

Appellants' invention results in reduced influences to the reactive component (specific protein) which is immobilized on the reactive layer, as well as reduced denaturation or deactivation of the reactive component (specific protein). Therefore, a chromatography medium with enhanced reactivity is achieved, due to enhanced permeation of the reactive layer and

uniform permeation of a sample, thus resulting in a chromatography measurement with a higher sensitivity and higher performance.

Additionally, by employing a surface active agent that is solidified when dried, the devitalization of the reactive component (specific protein) immobilized on the reactive layer can be minimized, thus realizing enhanced preservation stability, extended quality maintenance period and expanded storage condition of the chromatography medium. (See page 7, lines 14-19 of the disclosure.)

Further, by using a surface active agent which comprises sugar in a hydrophilic part, in addition to the advantages discussed above, the solubility is enhanced and the permeability is increased by the action of the sugar. Additionally, influence on the reactive component (specific protein) can be reduced, and the denaturization and devitalization of the immobilized protein can be minimized, resulting in a reactive layer which can perform for a long time. (See page 9, lines 1-11 of the disclosure.)

On the contrary, in a conventional immunochromatography device, a surface active agent is generally employed only for improving permeability of the reaction layer. When using a surface active agent which comprises no sugar in its hydrophilic part, and which is not solidified when dried, it is impossible to dry the surface active agent to an absolutely dry condition. This leads to gradually advanced devitalization of the immobilized antibody during the preservation period of the immunochromatography device, thereby deteriorating the performance of the material. This in turn unfavorably shortens the quality preservation period of the material and restricts the storage condition of the material. Therefore, when a surface active agent which comprises no sugar in its hydrophilic part and which is not solidified when dried is employed, it is impossible to provide a material with the high precision and high preservation stability which is achieved with Appellants' claimed chromatography medium.

There are three main causes for deterioration of the preservation stability of a chromatography medium in the analysis of a liquid sample.

(1) Deterioration of the permeability of the reaction layer of the chromatography medium, resulting in reduction of the liquid flow amount compared to the initial stage.

(2) Deterioration of the solvability of the marker reagent which is impregnated, and reduction of the amount of the marker reagent relating to the reaction compared to the initial stage.

(3) Deactivation of the marker reagent or the specific protein immobilized on the reaction layer.

The three causes discussed above result in a reduction in detection sensitivity, such as from 10 to 2 or 5, or a deterioration in precision, such as from CV5% to CV20%. (A CV value is a coefficient of variation, and a high CV value indicates a low quantitative performance.)

The object of the Appellants' invention is to provide a chromatography medium which can solve these problems, and which can maintain the performance of the chromatography medium at high sensitivity and high precision, even when the chromatography medium is stored for a long period of time. A chromatography medium which solves these problems is one which, for example, has a detection sensitivity of 10 at an initial state, and which maintains this detection sensitivity at a state unlimitedly close to 10 for a long period of time; as well as maintaining a measurement precision which was CV5% at an initial state, at a state unlimitedly close to 5%, for a long period of time.

In a chromatography medium, the reactive component is immobilized onto the reactive layer, thus, when using a chromatography medium to analyze a liquid sample (reactive component), maintaining the permeability of the reactive layer is very important. Surface active agent processing is often employed to avoid deterioration of the permeability of the reactive layer, as discussed in (1) above. Surface active agent processing is performed on the reactive layer in order to enhance permeability of the reactive layer, and thus enhance permeation performance of the chromatography medium. By enhancing the permeability of this reactive layer, the reactive layer can carry out development of a sufficient amount of liquid sample to the downstream region of the chromatography medium, even if the chromatography medium is stored for a long period of time.

Absorption of the marker reagent into the reactive layer during the maintenance period is a major cause of the deterioration of the solvability of the marker reagent, as discussed in (2) above. In order to solve this problem, surface active agent processing is often employed on the

impregnating part, or the surface active agent is mixed into the marker reagent. This method allows solvability of the marker reagent by suppressing the remaining amount of the marker reagent to the minimum, even when maintaining the permeability of the reaction layer for a long time.

However, the surface active agent, which is used to improve problems (1) and (2), discussed above, causes deactivation of the marker reagent or the protein which is immobilized onto the reactive layer.

The reactive component (specific protein) has a stereo-type structure which is made of fine strings, and is in a state where the stereo-type structure is likely to be destroyed. Specifically, when the reactive component (specific protein) is in solution, it is likely to be denatured or deactivated, because the bindings which support the stereo-type structure are likely to be separated from each other. On the other hand, the stereo-type structure is not likely to be destroyed in its dry state. Therefore, the preservation stability of the reactive component is naturally superior in its dry state compared to its solution state.

The surface active agent is likely to unfavorably affect the reactive component (protein). If a surface active agent which holds a little amount of water therein is employed, or one which is likely to absorb moisture from the environment is employed, then both the reactive layer and the reactive component (specific protein) which is immobilized on the reactive layer are also in a state which includes water. Therefore, the reactive component is likely to be denatured or deactivated, and will not withstand a long storage period. However, if the surface active agent is in a dry state, the reactive layer and the reactive component will also be in a dry state, and therefore it will be possible to maintain a long term preservation performance. Specifically, when the surface active agent is one which is solidified when dried, the reactive layer is in a completely dried condition until the liquid sample is applied thereto and permeates the reactive layer. Therefore, denaturation and deactivation of the reactive component (specific protein) can be minimized, resulting in enhanced preservation stability, extended quality maintenance and relaxation of storage conditions.

However, it is still very difficult to maintain the preservation performance for a long period of time, even in a dry state. In the food business, it is widely known to employ sugar as a

preservation agent in order to avoid the denaturation of proteins. However, even if the denaturation or deactivation of the protein is prevented, the solubility of sugar would result in deterioration of the permeability of the reaction layer.

Appellants' invention provides a surface active agent which is solidified when dried and has a sugar in its hydrophilic part, which is used to process the reactive layer, thereby preserving the permeability of the reactive layer for a long period of time as well as protecting the specific proteins by the function of sugar.

Arguments regarding Chu in view of Nanbu et al.

Chu relates to a method of assembling an analytical device that is used in the detection of a target substance in a liquid sample, and an assay using the analytical device. The invention of Chu comprises a surfactant-treated porous reaction membrane provided with at least one receptor area, which is in a limited region of the surfactant-treated porous reaction membrane. Chu teaches that the at least one receptor area has a higher concentration of surfactant than the areas of the sample-contacting surface that are peripheral to the limited region. (See column 1, lines 49-51 of Chu.) Further, Chu teaches that the surfactant causes the liquid sample to flow faster through the portions of the reaction membrane where receptor molecules are located. Therefore, since a higher concentration of surfactant is present in the receptor area in the porous reaction membrane, the liquid sample passes through this receptor area faster than through the periphery, thereby increasing the assay sensitivity. (See column 1, lines 60-64 of the reference.)

In other words, in the Chu patent, the enhancement of assay sensitivity at a reaction area of the reaction membrane is intended, and the reaction area is processed to include a higher concentration of surfactants than the other areas in the reaction membrane. This results in the liquid sample passing through the reaction area rapidly, so that the significant quantity of liquid sample can pass through the reaction area compared to its periphery, resulting in an increase of the assay sensitivity. Chu fails to teach or suggest enhancing the permeability of the reaction layer, maintaining long-term permeability of the reactive layer, processing the entire reaction layer with the surface active agent, or employing a particular surface active agent which is

solidified when dried and comprises sugar in a hydrophilic part to prevent denaturing or deactivation of the reactive component (protein).

The method of Chu does not teach or suggest processing the entire reaction layer with the surface active agent, in order to enhance the permeability of the entire reaction layer. On the contrary, Chu teaches reacting a particular area (the reaction area) to include a higher concentration of surfactant than the peripheral areas, thus teaching away from Appellants' claimed invention. Furthermore, Chu fails to teach or suggest employing a suface active agent which comprises sugar in a hydrophilic part, in order to prevent deactivation of the reactive component.

The teachings of Nanbu et al. fail to remedy the deficiencies of Chu.

Nanbu et al. disclose a method for measuring the concentration or the activity of UTI, wherein a urine sample, a buffer solution, a trypsin solution and a substrate solution are mixed and the trypsin activity is then measured, and wherein a surface active agent is included in either the buffer solution or the enzyme solution. Nanbu et al. further disclose that the use of the surfactant improves the protease activity, thereby improving the measurement sensitivity. (See column 2, lines 46-48 of Nanbu et al.) The reference also discloses that the UTI sensitivity is improved when using the surfactant mixed in the buffer solution, and that when the concentration of the surface active agent is increased, the UTI measurement sensitivity is also enhanced. (See column 7, lines 58-62 of Nanbu et al.)

First, as discussed above, Chu teaches processing a particular area with a high concentration of surfactants, rather than processing the entire reaction layer. Nanbu et al. do not teach or suggest altering the teachings of Chu to process the entire reaction layer with the surface active agent.

Second, Chu fails to teach or suggest using a surface active agent which comprises sugar in a hydrophilic part. Although Nanbu et al. teach a surface active agent having a sugar in its hydrophilic part as an example of surface active agent which enhances the activity of the protease, most of the examples of surface active agents which enhance the activity of protease are those which do not have sugar in their hydrophilic part. Nanbu et al. do not disclose or

suggest choosing a surface active agent which has sugar in its hydrophilic part in order to enhance the activity of the enzyme, or that the activity of the enzyme is enhanced by the function of the sugar in the hydrophilic part.

The Examiner does not provide a reason why one of ordinary skill in the art would select a surface active agent that is solidified when dried and comprises a sugar in a hydrophilic part. The Examiner asserts that he has taken notice of the equivalence of sucrose monolaurate (which contains a sugar in a hydrophilic part) to polyoxyethylene sorbitan monolaurate and polyoxyethylene sorbitan monooleate (which are taught in Chu). However, this assertion does not address Appellants' question as to why one of ordinary skill in the art would even choose sucrose monolaurate from the many surfactants taught by Nanbu et al. Even if the Examiner's assertion of equivalency is accurate, the Examiner has provided no reason why one of ordinary skill in the art would select this particular surfactant from the list provided in Nanbu et al. Further, the Examiner has provided no reason why one of ordinary skill in the art would select a surface active agent that is solidified when dried and comprises a sugar in hydrophilic part from the many surfactants disclosed by Nanbu et al. The Examiner asserts that he has taken notice of the equivalence of sucrose monolaurate to the surfactants of Chu. However, without a suggestion or motivation to select sucrose monolaurate from the list of surfactants in Nanbu et al., any equivalence between the surfactants is irrelevant.

Third, Nanbu et al. disclose that a surface active agent is employed in order to enhance the activity of the enzyme, and that the measurement sensitivity is enhanced by enhancing the activity of the enzyme. In other words, in the invention of Nanbu et al., the detection sensitivity which was 10 in the prior art is enhanced to a value such as 20 or 30. On the contrary, in Appellants' invention, the surface active agent is employed to enhance the permeability of the reaction layer, to maintain the permeability for a long period of time, and to prevent the denaturation or deactivation of reactive component (protein) by the function of the sugar in the hydrophilic part in long-term preservation thereby maintaining the performance of the specific protein. Specifically, Appellants' invention results in maintaining the detection sensitivity which is 10 at an initial state at a state unlimitedly close to 10 for a long period of time. Appellants' invention does not enhance the reaction activity of the specific protein.

Nanbu et al. do not teach or suggest employing a surface active agent in order to prevent the denaturation or deactivation of the enzyme, to enhance the preservation stability of the reagent solution, or to maintain the detection sensitivity.

Fourth, the Examiner asserts that one of ordinary skill in the art would have a reasonable expectation of success using the surface active agent (surfactants) of Nanbu et al. which is an equivalent of the surface active agent of Chu in place of the surface active agent of Chu.

However, if a surfactant such as n-octyl-β-D-thioglucoside or sucrose monolaurate, as taught in Nanbu et al., is employed in Chu, since the effect of these surfactants taught in Nanbu et al. is enhancement of the activity of the enzyme, the effect which is presumed when Nanbu et al. is combined with Chu is an enhancement of assay sensitivity of the receptor area on the reaction membrane. Specifically, the activation of the reaction between the target substance and the receptor area, i.e., the antigen-antibody reaction. Particularly, when Chu and Nanbu et al. are combined, one of ordinary skill in the art would expect enhancement of the reaction activity of the specific protein, or enhancement of the detection sensitivity, i.e., enhancing the detection sensitivity to a value such as 20 or 30 which is higher than 10.

There is no suggestion of the expectation of maintaining long-term permeation, or prevention of denaturation or deactivation of specific protein by the function of sugar in the hydrophilic part in long term preservation thereby maintaining the performance of the specific proteins, i.e., preserving the detection sensitivity which was 10 at an initial state in a state unlimitedly close to 10 for a long period of time.

Accordingly, the present invention which reduces the influences to the specific proteins which are immobilized to the reaction layer by using a surface active agent having sugar in a hydrophilic part and being able to become solid when dried is a new immuno-chromatography apparatus invented by the present inventors. Appellants' invention results in the following advantages: suppression of the denaturation or deactivation of the specific proteins to the minimum, enhancement of the preservation ability, lengthening of the quality preservation period, and relaxation of the maintenance conditions of the chromatography medium.

In summary, Appellants' claimed invention is patentable over the combination of Chu and Nanbu et al. for the following reasons:

1. Chu teaches processing a particular part of the reactive layer to contain a higher concentration of surfactants than the other areas, in order to increase assay sensitivity. Appellants' invention processes the entire reactive layer, rather than a portion of the reactive layer, with a surface active agent. The teachings of Nanbu et al. fail to remedy this deficiency.

2. Chu fails to teach or suggest a surface active agent which is solidified when dried and comprises a sugar in its hydrophilic part. Nanbu et al. disclose a long list of surfactants, which includes sucrose monolaurate. However, there is no motivation to choose this particular surfactant from the many disclosed by Nanbu et al. Therefore, whether this surfactant is equivalent to those taught by Chu is irrelevant.

3. Nanbu et al. teach improving measurement sensitivity, while Appellants' invention maintains measurement sensitivity.

4. The combination of references does not teach or suggest a chromatography medium which maintains long-term permeation, and which prevents the denaturation or deactivation of a specific protein by the function of sugar in the hydrophilic part for long term preservation, thereby maintaining the performance of the specific protein.

Arguments regarding Chu in view of Uenoyama et al.

Uenoyama et al. provide a method of measuring the in-urine protease obstruction substance by mixing a urine sample, a protease solution, and buffer solution, adding a substrate solution thereto to cause the enzyme reaction, and measuring the activity of the enzyme. The adjustment of the substrate solution is carried out by solving the substrate in an organic solvent, and adding at least one surface active agent, chosen from either an amphoteric surfactant or a nonionic surfactant, into a solution comprising at least one of an organic solvent and an aqueous medium.

This method employs a surface active agent in order to solve the slightly soluble substrate which is soluble by an organic solvent by using the organic solvent which is likely to inhibit the activity of the enzyme at minimum that is required, and in order to not precipitate the substrate. Further, the surface active agent is used so that the amount of an organic solvent can

be reduced, and a slightly soluble substrate can be used in a sufficient amount. (See column 3, lines 21-24 of Uenoyama et al.)

Additionally, because the substrate can be used in a sufficient amount, precision and reproducibility of the measurement can be improved. Further, by the use of the specific surfactants, the solubility of the substrate is also improved, so that crystallization of the substrate can be prevented. (See column 3, lines 24-31 of Uenoyama et al.) It is also described that if the nonionic surfactants are not used, the substrate crystallizes. (See column 9, lines 28-31 of Uenoyama et al.)

In Uenoyama et al., by using the surface active agent in order to enhance the solubility of the substrate, the amount of organic solvent which inhibits the activity of the enzyme by denaturing or deactivating the enzyme can be reduced, and as a result, the denaturation or deactivation of enzyme is suppressed and the activity and measurement sensitivity of the enzyme is enhanced. Although Uenoyama et al. teach a surface active agent which has sugar in its hydrophilic part as an example, most of the examples of surface active agents are those which do not have sugar in their hydrophilic part. It is clear that the measurement sensitivity is not necessarily enhanced by the function of the surface active agent having sugar in its hydrophilic part. Further, the role of the surface active agent in Uenoyama et al. is the enhancement of solubility of the slightly soluble substrate and the reduction of use amount of organic solvent.

The surface active agent in the present invention is intended to enhance the permeability of the reaction layer as well as to maintain the permeability for a long period of time, to preserve the performance of the specific protein by preventing the denaturation or deactivation of the specific protein by the function of sugar in the hydrophilic part in the long-term preservation. Appellants' invention does not suggest that the reaction activity of the specific protein is enhanced, or that the detection sensitivity which was 10 in the prior art is enhanced to a higher value. On the contrary, even if Uenoyama et al. is considered to suggest that the surface active agent functions indirectly as preventing the denaturation or deactivation of enzyme, it is absolutely an indirect function, and it is not directly contributing to the enhancement of the enzyme activity. Also, there is neither disclosure nor suggestion that the surface active agent is employed as the reagent enhancing preservation stability in order to preserve the reagent for the

long term, or that the surface active agent enhances the preservation stability of the enzyme solution by protecting the enzyme by sugar in the hydrophilic part.

The teachings of Uenoyama et al. do not remedy the deficiencies of Chu.

Initially, as discussed above, Chu teaches processing a particular area with a high concentration of surfactant, rather than processing the entire reaction layer. Uenoyama et al. do not teach or suggest altering the teachings of Chu to process the entire reaction layer with the surface active agent.

Second, Chu fails to teach or suggest a surface active agent comprising sugar in a hydrophilic part. The Examiner has not provided a reason why one of ordinary skill in the art would select a surface active agent that is solidified when dried and comprises a sugar in a hydrophilic part from the 16 types of surfactants disclosed by Uenoyama et al. The Examiner argues that n-octyl-B-D-thioglucoside and sucrose monolaurate are equivalent to the surface active agents taught by Chu. However, this response does not address Appellants' question as to why one of ordinary skill in the art would even choose n-octyl-B-D-thioglucoside or sucrose monolaurate from the many surfactants taught by Uenoyama et al. Even if the Examiner's assertion of equivalency is accurate, the Examiner has provided no reason why one of ordinary skill in the art would select this particular surfactant from the many surfactants disclosed in Uenoyama et al. Further, the Examiner has provided no reason why one of ordinary skill in the art would select a surface active agent that is solidified when dried and comprises a sugar in hydrophilic part from the many surfactants disclosed by Uenoyama et al. Although the Examiner asserts that n-octyl-B-D-thioglucoside or sucrose monolaurate are equivalent to the surfactants of Chu, without a suggestion or motivation to select n-octyl-B-D-thioglucoside or sucrose monolaurate from the list of surfactants in Uenoyama et al., any equivalence between the surfactants is irrelevant.

Third, the Examiner asserts that one skilled in the art would have expected success by employing a surface active agent of Uenoyama et al., which is an equivalent of the surface active agent of Chu, in place of the surface active agent of Chu.

The effect of these surface active agents taught in Uenoyama et al. is enhancement of solubility of a slightly soluble substrate, and thereby it is intended that the use amount of organic solvent is reduced and the activity of the enzyme is indirectly enhanced. However, there is no slightly soluble substrate or organic solvent used in Chu, and therefore there is no reason to employ a surface active agent which is intended to enhance the solubility of a slightly soluble substrate, as taught by Uenoyama et al.

Because one of ordinary skill in the art would not employ a component intended to enhance the solubility of a slightly soluble substrate when the device does not contain a slightly soluble substrate, it is impossible to predict a result. Further, it is impossible to expect long-term permeation preservation, or the preservation of the performance of the specific protein by preventing the denaturation and the deactivation of the specific protein by the function of sugar in the hydrophilic part in long-term preservation.

Accordingly, the present invention which reduces the influences to the specific proteins which are immobilized to the reaction layer by using the surface active agent having sugar in a hydrophilic part and being able to become solid when dried condition is a new immuno-chromatography apparatus invented by the present inventors. Appellants' invention results in the following advantages: suppression of the denaturation or deactivation to the minimum, enhancement of the preservation stability, lengthening of the quality preservation period, and relaxation of the maintenance.

In summary, Appellants' claimed invention is patentable over the combination of Chu and Uenoyama et al. for the following reasons:

1. Chu teaches processing a particular part of the reactive layer to contain a higher concentration of surfactants than the other areas, in order to increase assay sensitivity. Appellants' invention processes the entire reactive layer, rather than a portion of the reactive layer, with a surface active agent. The teachings of Uenoyama et al. fail to remedy this deficiency.

2. Chu fails to teach or suggest a surface active agent which is solidified when dried and comprises a sugar in its hydrophilic part. Uenoyama et al. disclose 16 types of surfactants, which include n-octyl-B-D-thioglucoside or sucrose monolaurate. However, there is no

motivation to choose one of these particular surfactants from the many disclosed by Uenoyama et al. Therefore, whether these surfactants are equivalent to those taught by Chu is irrelevant.

3. Uenoyama et al. employ a surface active agent in order to enhance the solubility of a slightly soluble substrate. However, there is no slightly soluble substrate or organic solvent used in Chu, and therefore there is no reason to employ a surface active agent which is intended to enhance the solubility of a slightly soluble substrate, as taught by Uenoyama et al.

4. The combination of references does not teach or suggest that the surface active agent is employed as the reagent enhancing preservation stability in order to preserve the reagent for the long term, or that the surface active agent enhances the preservation stability of the enzyme solution by protecting the enzyme by sugar in the hydrophilic part.

For these reasons, the invention of claims 5, 12, 27, 31, 41, 45, 53 and 60 is clearly patentable over Chu in view of Nanbu et al. or Uenoyama et al.

Rejection under 35 U.S.C. § 103(a) over Chu in view of Nanbu et al. or Uenoyama et al. and further in view of Iwata et al. (U.S. 5,912,139)

Claim 49 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Chu in view of Nanbu et al. or Uenoyama et al. and further in view of Iwata et al. (U.S. 5,912,139).

The comments set forth above are equally applicable to this rejection. Since claim 49 is directly dependent on claim 12, the subject matter of claim 49 is patentable over Chu in view of Nanbu et al. or Uenoyama et al. for the same reasons that the subject matter of claim 12 is patentable over this combination of references. The teachings of Iwata et al. do not remedy the deficiencies of these references.

Thus, the subject matter of claim 49 is patentable over the teachings of Chu in view of Nanby et al. or Uenoyama et al. and further in view of Iwata et al.

VIII. CONCLUSION

For the foregoing reasons, claims 5, 12, 27, 31, 41, 45, 49 53 and 60 are patentable over the cited references. Thus, reversal of the final rejection is respectfully requested.

Attached herewith are a Claims Appendix, an Evidence Appendix, and a Related Proceedings Appendix.

The brief is submitted with the requisite fee of $500.00.

Respectfully submitted,

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CLAIMS APPENDIX

1-4. (Cancelled)

5. (Appealed) A chromatography medium which comprises a reactive layer on which at least one reactive component for a chromatographic analysis is immobilized,

wherein the reactive layer includes a surface active agent that is solidified when dried, and

wherein the surface active agent comprises a sugar in a hydrophilic part of the surface active agent.

6-11. (Cancelled)

12. (Appealed) A method for manufacturing a chromatography medium which comprises a reactive layer on which at least one reactive component for a chromatographic analysis is immobilized comprising:

(a) impregnating or coating the reactive layer of the chromatography medium with a liquid, wherein a surface active agent which is solidified when dried is dissolved in the liquid; and

(b) drying the reactive layer which has been impregnated or coated with the liquid in which the surface active agent is dissolved,

wherein the surface active agent comprises a sugar in a hydrophilic part of the surface active agent.

13-26. (Cancelled)

27. (Appealed) The chromatography medium as defined in Claim 5,

wherein the reactive layer comprises the surface active agent in the entirety of the reactive layer.

28-30. (Cancelled)

31. (Appealed) The chromatography medium as defined of Claim 5,

wherein the reactive layer comprises the surface active agent in a part of the reactive layer.

32-40. (Cancelled)

41. (Appealed) The method for manufacturing a chromatography medium as defined in Claim 12,

wherein the reactive layer is dried by air drying.

42-44. (Cancelled)

45. (Appealed) The method for manufacturing a chromatography medium as defined in Claim 12,

wherein the reactive layer is dried by wind drying.

46-48. (Cancelled)

49. (Appealed) The method for manufacturing a chromatography medium as defined in Claim 12,

wherein the reactive layer is dried by freeze drying.

50-52. (Cancelled)

53. (Appealed) The method for manufacturing a chromatography medium as defined in Claim 12,

wherein the entire reactive layer is impregnated or coated with the liquid in which the surface active agent is dissolved.

54-59. (Cancelled)

60. (Appealed) The method for manufacturing a chromatography medium as defined in Claim 12,

wherein a part of the reactive layer is impregnated or coated with the liquid in which the surface active agent is dissolved.

61-63. (Cancelled)

EVIDENCE APPENDIX

NONE

RELATED PROCEEDINGS APPENDIX

NONE